

## JOURNAL EDITOR-IN-CHIEF'S REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 82589

**Title:** Human retinal secretome: A cross link between mesenchymal and retinal cells

**Journal Editor-in-Chief (Associate Editor):** Shengwen Calvin Li

**Country/Territory:** United States

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SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	language polishing	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Major revision

### JOURNAL EDITOR-IN-CHIEF (ASSOCIATE EDITOR) COMMENTS TO AUTHORS

EIC Specific comments 1) Introduction: The authors need to define the term: EVs, exosomes, microvesicles, secretome, etc. They need to follow those circumstances in citations strictly. Don't blend them in to create confusion. E.g., on page 7, "During the last few years, it has been revealed that MSCs are able to modify the microenvironment by releasing EVs, primarily distinct into apoptotic bodies, micro-vesicles and exosomes[22]." A table should be used to distinguish them. 2) Figure 1 did not match the content of Table 1. For example, in Fig 1, PDGF is an overlapped molecule among MSC, retinal, and mesenchymal cell secretomes, but not in Table 1 (Retinal cell secretome). Check all that apply to corresponding Fig 1 and Table 1. 3) Fig 1. More descriptive illustrations should be applied in the figure legend. Such as three panels: label with A, B, and C, and follow with descriptions, such as the retinal structure of multiple-cell layers. Why did they mark "0" in MSC in the circle? 4) Table 1 should be given citations for all biomarkers. 5) In the abstract, "we have delineated the importance of crosstalk between mesenchymal stem cells and retinal cells" – they need to uplift and elaborate concretely on the importance of such a crosslink – the main point of the

literature review, such as what is the uniqueness of the crosslink? 6) In the Introduction, they stated, "In this review, we try to link the secretome of MSCs to the retinal cell secretome in order to highlight the state of the art of secreted factor involvement in retinal diseases." However, in Conclusion, they did not drive the homerun back to the highlights of what factors are unique for crosslinks. Such cohesiveness is a must in transition. 7) Why did the authors focus on the identical biomarkers among overlapped molecules (Fig 1) among MSC, retinal, and mesenchymal cell secretomes? Did they not think complementary biomarkers play a functional compensation role given "thanks to released soluble paracrine bioactive components and extracellular vesicles?" Why did they apply for MSC on eye care? Specifically, A table summarized from ClinicalTrials.gov should be used to guide the readers as this is a Web-based resource that provides patients, their family members, healthcare professionals, researchers, and the public with easy access to information on publicly and privately supported clinical studies on a wide range of diseases and conditions. As they stated on page 6, "Today, preclinical and clinical trials using MSCs have been performed in different kinds of pathologies with promising results, such as autoimmune disease, joint reconstruction, vascular disease, nerve injury, organ transplantation, degenerative disease and severe infection[14]." They need always specify what kind of MSCs. 8) Use cross-link or crosslink to replace two word phrase "cross link" [in the Title] across the page. 9) Page 4: "knowledge on of released factors' mechanisms of action during their potential beneficial role." Use adv. Potentially, not adj. potential, as it modifies an adj. [beneficial]. 10) Page 5: "MSC isolation is a noninvasive process, and this represents a fundamental advantage also from an ethical and/or legal point of view[6]." How did they define "non-invasive?" Don't use MSC, in a generic, but be specific. On pages 9-10, "BM-MSC-EVs, MSC-EVs-PD- and hUCMSCs-EVs also exhibited a healing role in autoimmune conditions[45]. miR-146a and miR-27a/b," 11) Page 6: "The secretome released by MSCs consists of a condition medium (CM) made up of soluble" - use the conditioned medium. 12) Page 10: "The most intriguingly aspect of secretome EV fractions probably deals with functional mitochondria release from human mesenchymal stromal cells[52]." Use an adj. [intriguing], not an adv. [intriguingly] in front of a Noun [aspect]. 13) Page 12: "synuclein aggregates, through a MMP-2-based mechanism[65]." Use an not a in front of MMP. 14) Many grammar errors crawl across the pages.